HOMEOSTASIS, REGULATION, STRESS

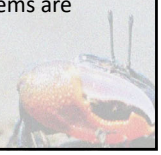
We have so far examined key factors that affect how animals work

- adaptations to their environment.
- body size and shape (particularly mass)
- phylogenetic relatedness

Next we will look at the major body "systems"

- metabolism
- ambient and body temperature
- ionic and osmotic balance
- respiration and circulation

But first we will look at some core concept regarding how many of these systems are regulated (or not).



1

Homeostasis, Regulation, Stress

Homeostasis is a self-regulating process by which biological systems maintain stability while adjusting to changing external conditions.

(Billman 2020 https://doi.org/10.3389/fphys.2020.00200)

In all animals, there are internal regulatory mechanisms that keep the internal environment constant.

Interactions of animals with their environment (especially stressful environments) can perturb internal homeostasis, and animals must minimise the impact of environmental stress (The bulk of all environmental physiology lectures).

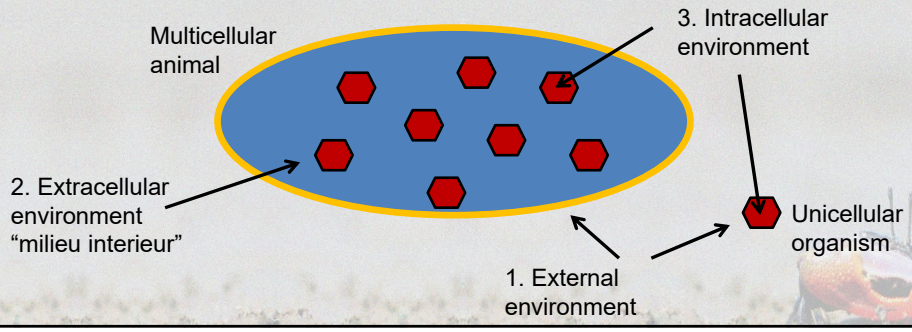
Neural and endocrine control systems are major internal regulatory mechanisms.

2

For multicellular animals there are three "environments"

- External environment – the "outside world"
- Extracellular environment
- Intracellular environment

Internal environments

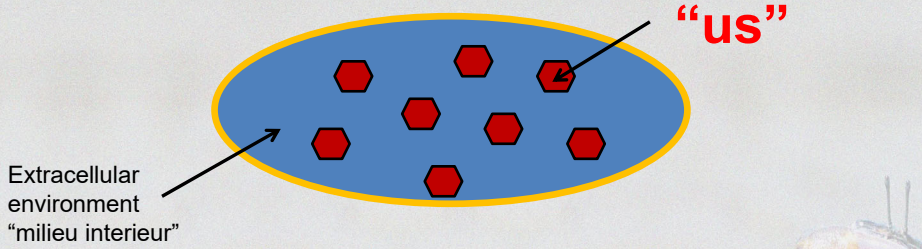


3

Extracellular Homeostasis

Walter Cannon on the constancy of the extracellular environment:

"so long as this personal, individual sack of salty water, in which each one of us lives and moves and has his being, is protected from change, we are freed from serious peril"



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Extracellular Homeostasis

Extracellular homeostasis is constancy:
but constancy can be achieved in different ways!

1. Passive equilibrium
2. Steady-state homeostasis
3. Negative feedback regulation

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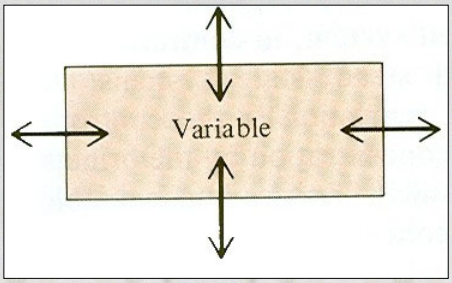
Equilibrium homeostasis:

Passive

No regulatory mechanism.

Equilibrium of the external and internal environments.

e.g. icefish T_b



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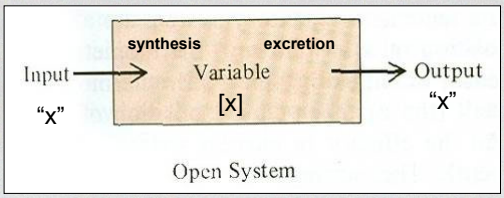
Steady-state homeostasis:

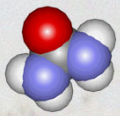
Open system – no apparent regulatory mechanism

e.g. Substance "x" enters the body fluids at a particular rate, and elimination of x is dependant on its concentration in the body fluids.

Rate of elimination = Rate of release.



e.g. blood concentration of urea



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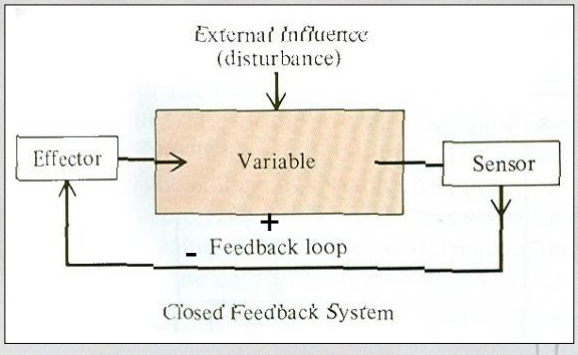
Negative Feedback Homeostasis:

Specific physiological mechanism for regulation.

- sensor
- setpoint
- error
- effector
- negative feedback



- Closed loop
- Effector opposite (negative) to Disturbance

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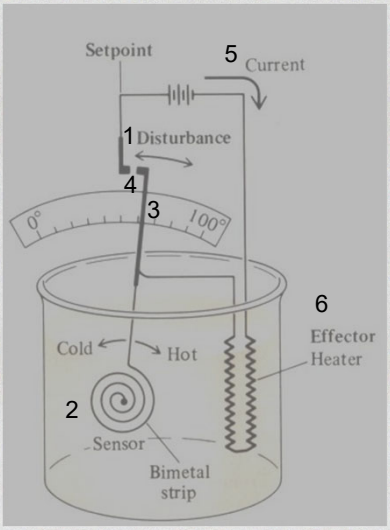
Simple Example – a water bath



1. Disturbance (T_{water})
2. Sensor
3. Setpoint
4. Error
5. Feedback
6. Effector

This is a simple
One-way (only heats)
On/off control system

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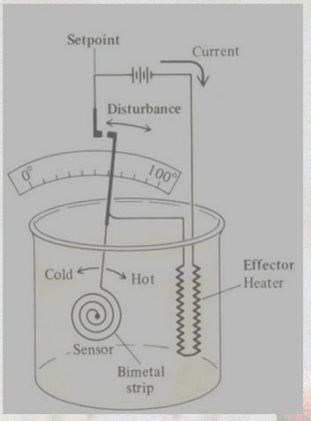
Regulatory Mechanisms

On-Off control:

The effector response is only turned ON or OFF

This reduces the
precision of feedback
and increases the
likelihood of oscillations

This simplicity is uncommon
in physiological control



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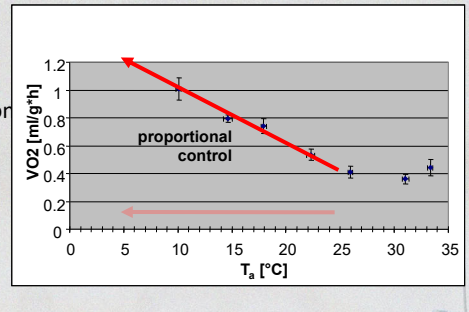
Regulatory Mechanisms

Proportional control:

The effector response can be proportional to the error term
This increases the precision of feedback
and minimises oscillations
e.g. T_b regulation

in mammals by metabolic heat production



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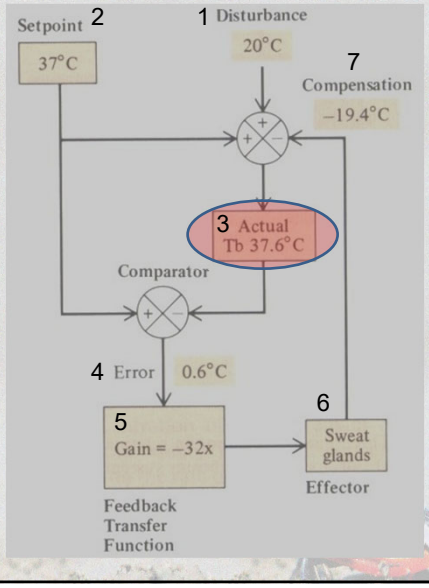
Body Temperature Regulation
e.g. when it is hot: Disturbance = +20 oC

Disturbance is +20 ºC
Setpoint is 37 ºC
Tb actual is 37.6 ºC
Comparator:Error is 0.6 ºC
GAIN = - 19.4/0.6
= - 32
Effector is sweating
Compensation is -19.4 ºC

THIS IS STEADY-STATE
disturbance = error - compensation



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How does that work??!!

Setpoint + Disturbance + Compensation = T_b

Setpoint is 37 ºC

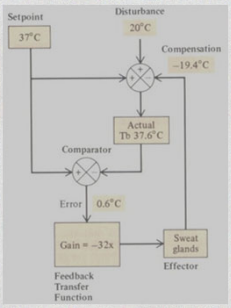
Disturbance is +20 ºC

T_b is X ºC ??????

Error is (X – 37) ºC

Gain is -32

Compensation is -32 [X-37]



T_b = Setpoint + Disturbance + Compensation

$T_b = 37 + 20 + (-32\ [Tb - 37])$

$T_b = 57 - 32\ T_b + 1184$

$33\ T_b = 1241$

$T_b = 37.606$

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T_b Regulation when it is cold
Disturbance = -20 oC

Setpoint is 37 ºC

Disturbance is -20 ºC

Tb is X ºC ?????

Gain is -32

Error is (X - 37) ºC

Compensation is -32 (X-37) ºC

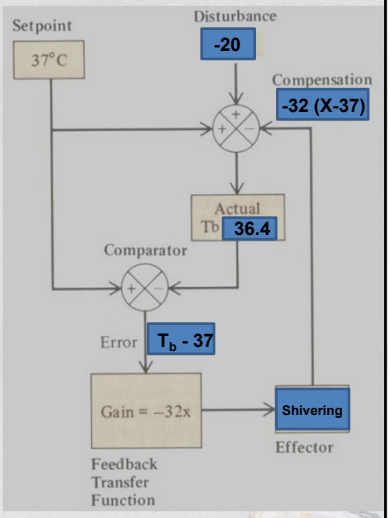
Set + Comp + Disturbance = T_b

$T_b = 37 - 20 + (-32)(T_b - 37)$

$T_b = 17 - 32\ T_b + 1184$

$33\ T_b = 1201$

$T_b = 36.394$



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T_b Regulation in general (if Disturbance = T_a – 37)

Setpoint is 37 ºC

Disturbance is [T_a-37] ºC

T_b is ???? ºC

Gain is -32

Error is X - 37 ºC

Compensation is -32 [X–37] ºC

Set + Disturb + Comp = T_b

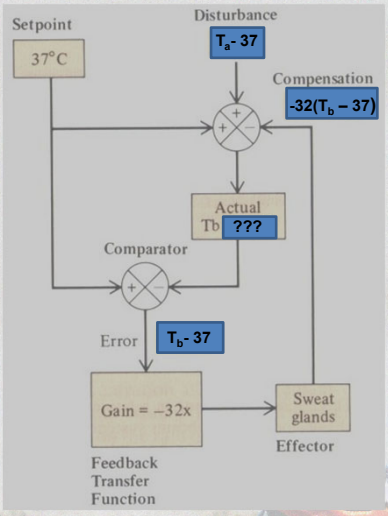
$T_b = 37 + [T_a\text{-}37] + (-32)(T_b\text{-}37)$

$T_b = 37 + [T_a\text{-}37] - 32T_b + 1184$

$33\ T_b = 1221 + [T_a\text{-}37]$

$T_b = 37 + (1/33)\ [T_a\text{-}37]$

$T_b = (1184/33) + (1/33)\ T_a$



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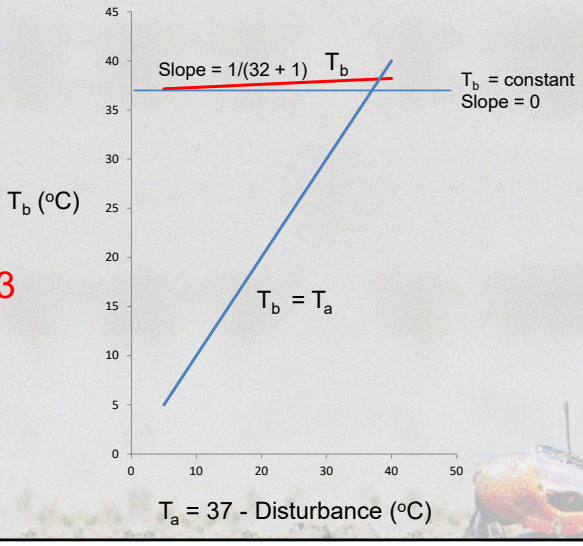
T_b is not regulated constant!? (at least by simple negative feedback)

Disturbance	Tb
5	37.15152
10	37.30303
15	37.45455
20	37.60606
25	37.75758
30	37.90909
35	38.06061
40	38.21212

$T_b = (1184 + T_a)/33$



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Regulatory Mechanisms

Sometimes we have multiple control systems:

- Several different regulatory effectors may operate to control variables
- This provides more precise regulation but requires complex sensory, feedback and effector systems

  e.g. thermoregulation in mammals and birds by metabolism, vasomotion, posture, insulation, sweating, panting, salivation, etc

  e.g. behavioural T_b regulation by a lizard. Both a high T_b setpoint and a low T_b setpoint. Precision depends on how close upper and lower setpoints are.

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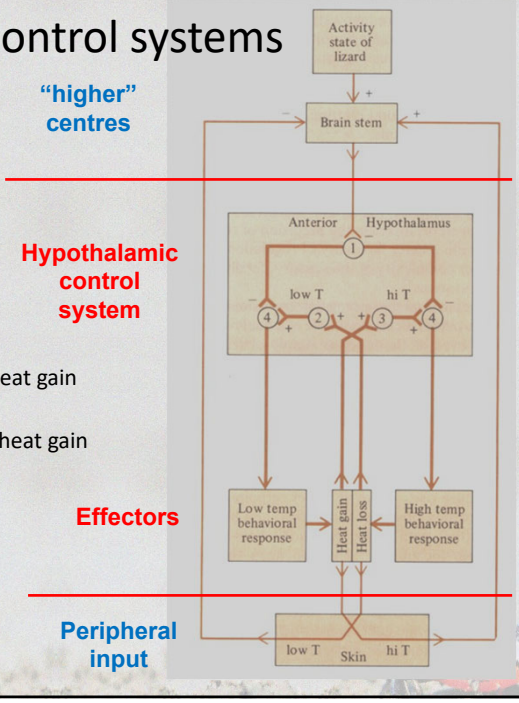
Multiple control systems

Heliothermic lizards

Low temperature response increases heat gain (e.g. basking)

High temperature response decreases heat gain (e.g. seeks shade)



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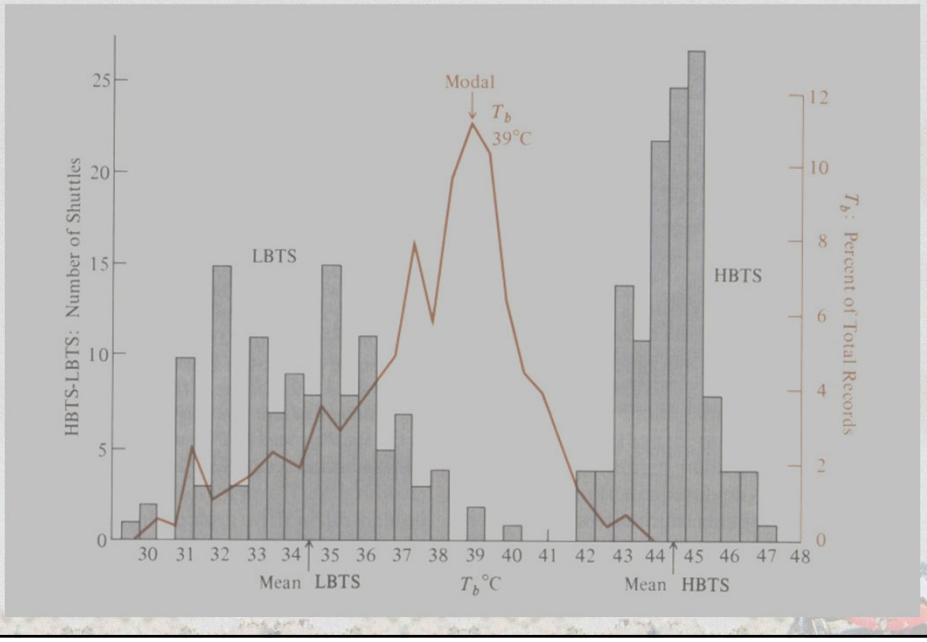
Dual-thermostat system



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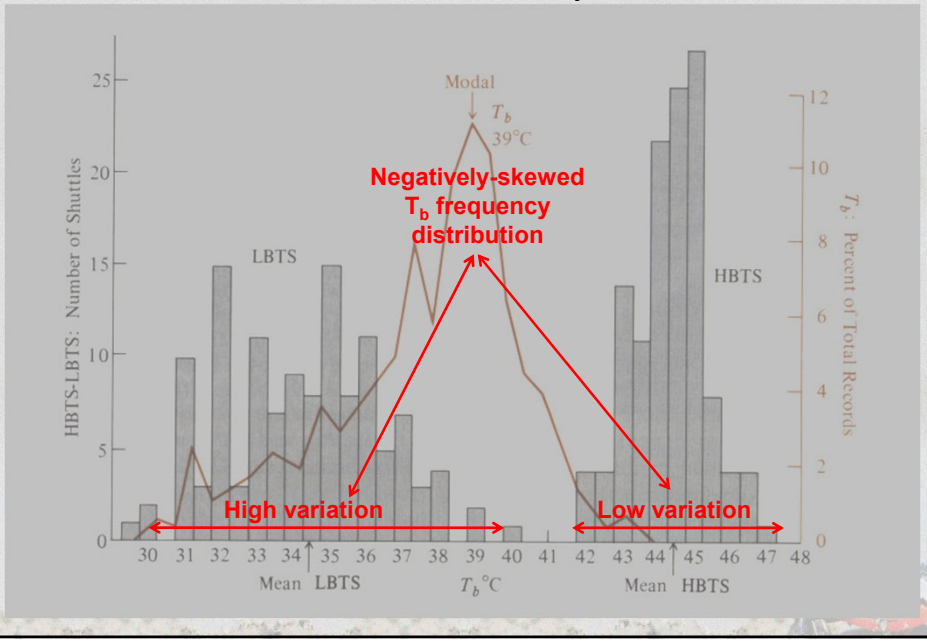
Dual-thermostat system



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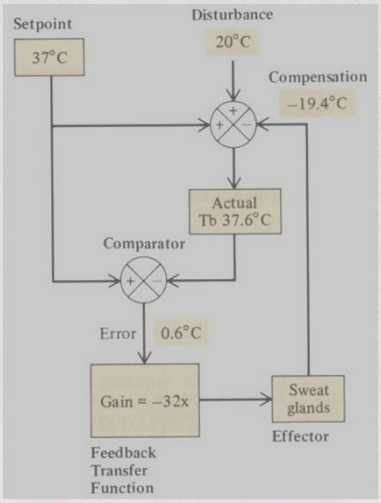
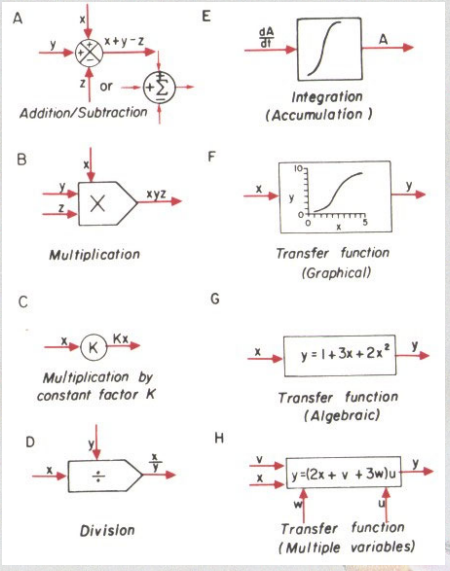
Control System Schematics



Control Functions



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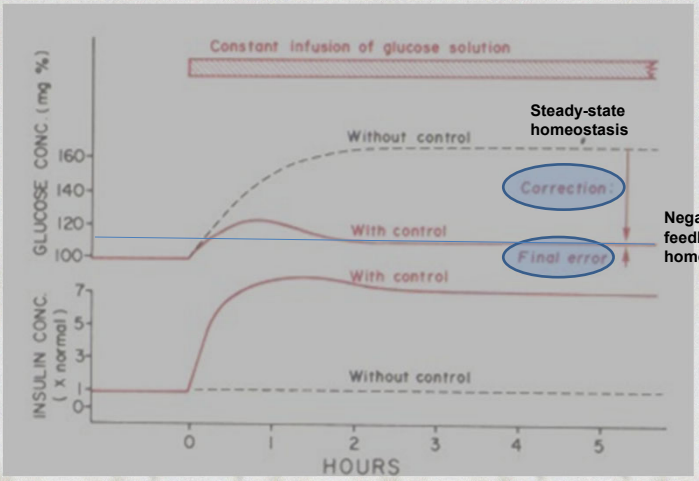
e.g. Blood glucose regulation



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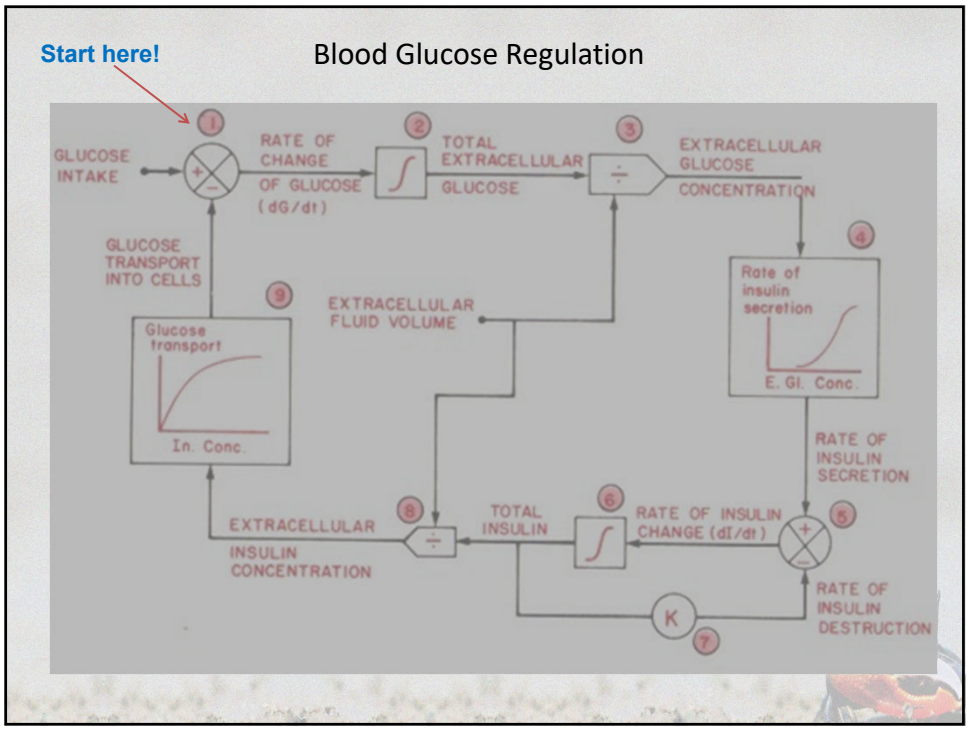
Start here!
Blood Glucose Regulation
GLUCOSE INTAKE
RATE OF CHANGE OF GLUCOSE (dG/dt)
TOTAL EXTRACELLULAR GLUCOSE
EXTRACELLULAR GLUCOSE CONCENTRATION
GLUCOSE TRANSPORT INTO CELLS
Glucose transport
In. Conc.
EXTRACELLULAR FLUID VOLUME
Rate of insulin secretion
E. Gl. Conc.
RATE OF INSULIN SECRETION
EXTRACELLULAR INSULIN CONCENTRATION
TOTAL INSULIN
RATE OF INSULIN CHANGE (dI/dt)
RATE OF INSULIN DESTRUCTION
K

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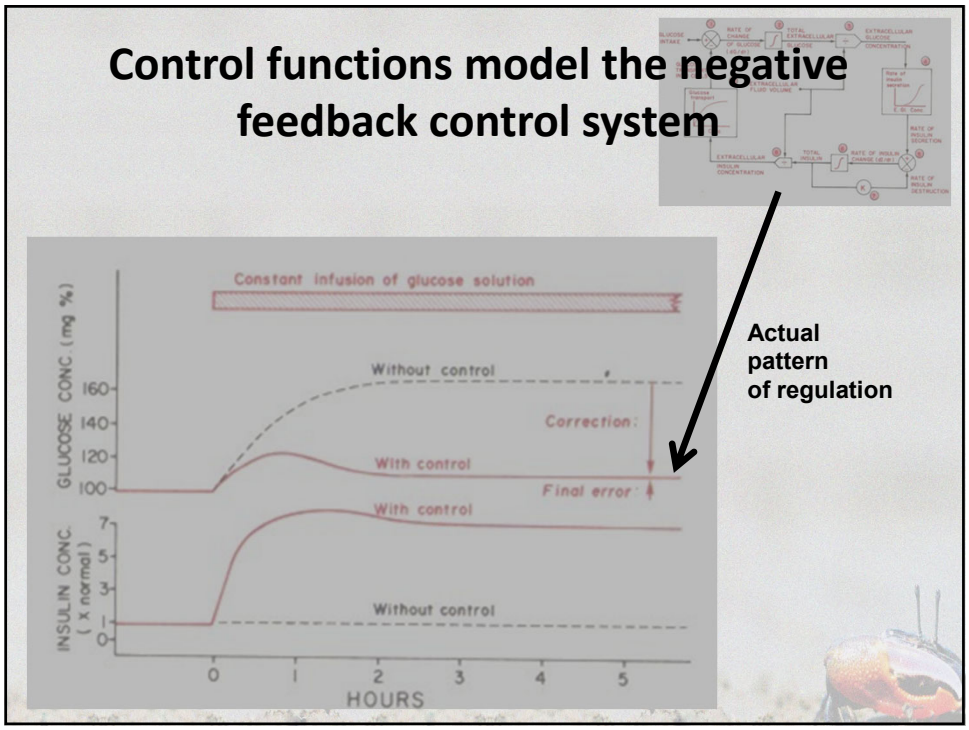
Control functions model the negative feedback control system
Constant infusion of glucose solution
GLUCOSE CONC. (mg %)
Without control
Correction
With control
Final error
INSULIN CONC. (X normal)
With control
Without control
HOURS
Actual pattern of regulation

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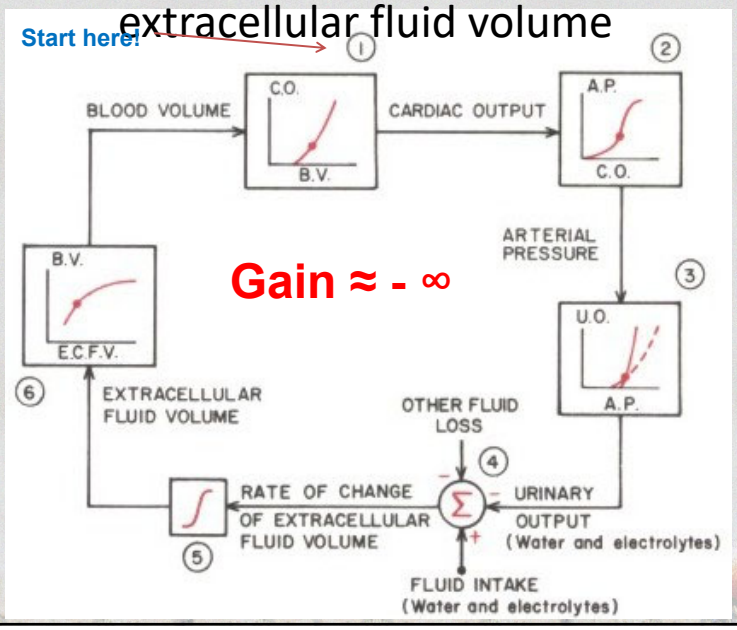
A “perfect” regulation system: extracellular fluid volume



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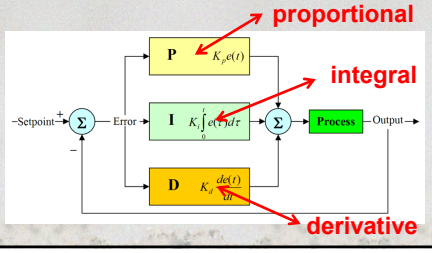
PID control - Proportional-Integral-Derivative

Modern electronic control systems

- have proportional control
- integrate the error term over time to completely eliminate it.
- Use the derivative (rate of change) to make the adjustment quicker



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Feed-forward Control

Feed-forward control describes a pathway within a control system that uses a signal from the external environment to anticipate change ("derivative")

Such a control system with feed-forward behavior responds to its control signal in a pre-defined way before responding to how the load reacts.

e.g. anticipatory regulation of heartbeat in advance of actual physical exertion

e.g. skin temperature increases with solar radiation before core T_b changes

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Positive feedback – Bad?!

Compensation usually counteracts the disturbance.

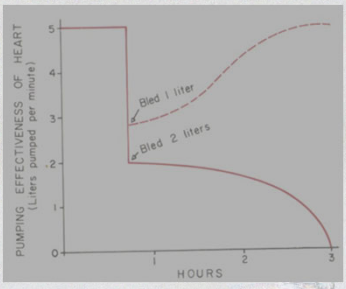
If compensation augments the disturbance

De-stables homeostasis – bad if you want homeostasis

e.g. Blood pressure regulation with blood loss

Moderate blood loss (1 L) decreases cardiac output (hence blood pressure) but compensatory mechanisms (vasoconstriction) are adequate to restore blood pressure.

Excessive blood loss (2 L) reduces blood flow to the brain, which suppresses compensatory mechanisms and this leads to positive feedback and rapid cardiovascular collapse.



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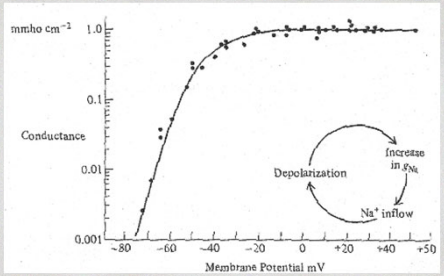
Positive feedback – can be Good

De-stabilised homeostasis – can be used for beneficial functions and/or required rapid changes

e.g. action potential by a nerve or muscle cell (depolarisation of membrane potential increases Na+ and leads to further depolarisation).



e.g. endocrine regulation of reproduction - oestrogen secretion increases luteinizing hormone, which further increases oestrogen secretion.

e.g. vomiting, birth, emptying bladder

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